Implementing a Standardized Perioperative Antibiotic Prophylaxis Protocol for Neonates Undergoing Cardiac Surgery

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Background. A lack of perioperative antibiotic prophylaxis guidelines for neonates undergoing cardiac surgery has resulted in a wide variation in practice. We sought to do the following: (1) Determine the safety of a perioperative antibiotic prophylaxis protocol for neonatal cardiac surgery as measured by surgical site infections (SSIs) rates before and after implementation of the protocol; and (2) evaluate compliance with selected process measures for perioperative antibiotic prophylaxis.

Methods. This quasi-experimental study included all cardiac procedures performed on neonates from July 2009 to June 2012 at a single center. An interdisciplinary task force developed a standardized perioperative antibiotic prophylaxis protocol in the fourth quarter of 2010. The SSI rates were compared in the preintervention (July 2009 to December 2010) versus the postintervention periods (January 2011 to June 2012). Compliance with process measures (appropriate drug, dose, timing, and discontinuation of perioperative antibiotic prophylaxis) was compared in the 2 periods.

Results. During the study period, 283 cardiac procedures were performed. The SSI rates were similar in the preintervention and postintervention periods (6.21 vs 5.80 per 100 procedures, respectively). Compliance with the 4 process measures significantly improved postintervention.

Conclusions. Restricting the duration of perioperative antibiotic prophylaxis after neonatal cardiac surgery to 48 hours in neonates with a closed sternum and to 24 hours after sternal closure was safe and did not increase the rate of SSIs. Compliance with selected process measures improved in the postintervention period. Additional multicenter studies are needed to develop national guidelines for perioperative prophylaxis for this population.


Surgical site infections (SSIs) are a serious health complication after operative procedures and are associated with increased mortality and health care costs [1]. The SSI rates after pediatric cardiac surgery range from 2.3% to 9.9% [2–7]. Thus, prevention of SSIs is a quality improvement metric for health care organizations, and state and federal regulatory bodies [8–14]. The Joint Commission has made the reduction of SSIs and implementation of evidence-based practices for prevention of SSIs, including appropriate use of perioperative prophylaxis, a national patient safety goal for 2013 [8]. Several national organizations including the Society of Thoracic Surgeons, the Centers for Disease Control and Prevention, American Society of Health-System Pharmacists, the Surgical Infection Society, the Infectious Diseases Society of America, and the Society for Health Care Epidemiology of America have developed guidelines for perioperative antibiotic prophylaxis after cardiac surgery [9–14].

However, current guidelines are largely restricted to adult populations as few studies describe the efficacy of perioperative antibiotic prophylaxis for children [11]. Thus, pediatric recommendations are largely based on expert opinion and from data extrapolated from adult patients [11]. As a result, there is wide variation in practice across pediatric cardiac centers; several different prophylactic antibiotic regimens are followed and for varying durations [15–21]. Despite lack of evidence of clinical benefit, extended antibiotic prophylaxis until removal of thoracotomy tubes or invasive lines remain common practices in pediatric populations [3, 15–21].

The Surgical Infection Prevention Project (SIP) was introduced in 2002 as a quality improvement initiative to promote optimal use of perioperative antibiotic prophylaxis [10]. The SIP adopted 3 processes of care measures to reduce SSIs; selection of appropriate antibiotic consistent with published guidelines, administration of parenteral antimicrobial prophylaxis within 60 minutes prior to skin incision, and discontinuation of antimicrobial prophylaxis within 24 hours of surgery and within 48 hours for cardiac surgery to reduce SSI. These evidence-based recommendations have been incorporated into the broader
Surgical Care Improvement Project, and adopted by the Joint Commission and other national quality improvement forums [10].

To date, evidence-based recommendations are unavailable for perioperative antibiotic prophylaxis for neonates who undergo cardiac surgery. We hypothesized that limiting prophylaxis to 48 hours as recommended for adult cardiac surgical patients would be safe in neonates. We present a protocol, developed at our institution by an interdisciplinary task force, for perioperative antibiotic prophylaxis for neonatal cardiac surgery. A quasi-experimental study of all neonates who underwent cardiac surgery was conducted with the following objectives: (1) To determine the safety of a perioperative antibiotic prophylaxis protocol for neonatal cardiac surgery as measured by SSI rates before and after implementation of the protocol; and (2) validate compliance with selected process measures for perioperative antibiotic prophylaxis.

Material and Methods

Study Design, Site, and Subjects

We performed a quasi-experimental study of neonates who underwent cardiac surgery from July 1, 2009 to June 30, 2012 at our tertiary care academic center in New York City. Some subjects were previously included in a study of risk factors for SSIs [22]. The SSIs were compared in the preintervention (July 1, 2009 to December 31, 2010) and postintervention (January 1, 2011 to June 30, 2012) periods. Included subjects were neonates 30 or less days of age who underwent cardiac surgery and received preoperative and postoperative care in the cardiac section of the neonatal intensive care unit (NICU). Excluded neonates were premature (<37 completed weeks of gestation) infants who underwent ligation of the ductus arteriosus only, in whom insertion of a permanent pacemaker was the only procedure performed (as the perioperative prophylaxis regimen is different), and who died within 24 hours after surgery. The Institutional Review Board for Columbia University Medical Center approved this study with a waiver of informed consent.

Perioperative Antimicrobial Prophylaxis Regimen

In the fourth quarter of 2010, after reviewing existing evidence, an interdisciplinary task force developed a consensus-based protocol for perioperative antibiotic prophylaxis for neonatal cardiac surgery. The task force included representatives from Departments of Pediatric Cardiothoracic surgery, Pediatric Cardiology, Neonatology, Pediatric Infectious Disease, Infection Prevention and Control, and Anesthesiology. The perioperative prophylaxis recommendations included the use of the appropriate antimicrobial agent, dose, timing of preoperative dose, intraoperative re-dosing (if relevant), and discontinuation (Table 1). After receiving institutional approval, the protocol was implemented on January 1, 2011. During the implementation period, the task force met quarterly and SSI rates and compliance with the prophylaxis recommendations data were shared.

During the preintervention period, the perioperative antimicrobial prophylaxis regimen was similar to that followed during the postintervention period with 3 exceptions. (1) For neonates who underwent lateral thoracotomy or median sternotomy whose sternal wound was closed in the operating room, cefazolin was continued until all chest tubes were removed. (2) For neonates whose sternal wound was left open, vancomycin and gentamicin were provided until sternal closure after which cefazolin was provided until all chest tubes were removed. (3) Prescriber audit and feedback of perioperative prophylaxis parameters were not performed.

Process of Care Measures

The interdisciplinary task force adopted the following 4 processes of care measures to assess compliance with the standardized protocol in the areas of correct drug, dose, timing, and discontinuation.

(1) Correct drug: as per protocol (Table 1).
(2) Correct dose for cefazolin or vancomycin: ±10% of recommended dose (Table 1).
(3) Correct timing: Preoperative, as per protocol (Table 1). Intraoperative re-dosing; cefazolin re-dosing should be initiated 4 hours ±30 minutes from previous dose or 8 hours ±30 minutes from previous dose if vancomycin is used. Postoperative, as per protocol (Table 1).
(4) Correct discontinuation: as per protocol (Table 1).

Case Definitions

The task force performed active surveillance for SSIs preintervention and postintervention. The Center for Disease Control and Prevention National Healthcare Surveillance Network definition for SSI was used [23]. Patients were followed for SSI for 90 days after the surgical procedure. The Pediatric Infection Prevention and Control, NICU, and cardiothoracic surgery teams detected potential SSIs. A member of the cardiac surgical team adjudicated cases (R.C.). If a patient had more than 1 surgical procedure, the SSI was attributed to the most recent procedure unless the procedure was performed secondary to infection (eg, debridement).

Data Collection

The following data were collected from each patient’s electronic medical record by a single investigator (M.M.): age at time of initial surgery; sex; weight; gestational age; risk adjustment in congenital heart surgery (RACHS-1) category; compliance with the 4 process measures for appropriate perioperative antibiotic prophylaxis; and SSI microbiology results, when available. The RACHS-1 groups cardiac surgical procedures with similar operative mortality rates into 6 categories with group 1 procedures carrying the lowest risk and group 6 procedures, the highest risk of mortality [24].
Statistical Methods
Descriptive analyses were completed to determine the incidence of SSI and compliance with the perioperative antibiotic prophylaxis guidelines. To ensure the comparability of the patient population in the preintervention and postintervention periods, characteristics of included neonates undergoing surgery during these 2 time periods were compared. For continuous and categoric characteristics, t tests and chi-squared tests were used to test for statistical significance, respectively. The proportions of appropriate perioperative antibiotic prophylaxis and the rate of SSI before and after protocol implementation were compared using chi-squared tests. Differences were considered significant for a p value 0.05 or less. Statistical analyses were conducted using SAS (9.2 for Windows; SAS Institute Inc, Cary, NC).

Results
During the study period, 305 neonates underwent 317 cardiac surgical procedures, of which 34 were excluded (Fig 1). In the final analysis, 283 procedures were included; 145 preintervention and 138 postintervention. Overall, the study population was similar during the preintervention and postintervention periods (Table 2). However, significantly more complex surgeries were performed during the postintervention period (p = 0.02).

Incidence of SSI During Preintervention and Postintervention Periods
During the study period, 17 SSIs (6.00 SSI per 100 procedures) were diagnosed; 14 were superficial and 3 were deep incisional SSIs. The rate of SSI was similar in the preintervention and postintervention periods (6.21 vs 5.80 per 100 procedures, respectively, p = 0.88). The median number of days to SSI was 20.0 (range 4 to 49 days) and did not differ significantly between the preintervention and postintervention periods (p = 0.53).

Pathogens Causing SSI
Methicillin-susceptible Staphylococcus aureus ( MSSA) was the most common pathogen during both study periods. MSSA caused 67% of SSI in the preintervention period and 38% of SSI during the postintervention period (p = 0.35).

Compliance With Perioperative Antibiotic Prophylaxis
The most common deficiencies noted during the Pre-intervention period were the following (Table 3): (1) 20% of patients did not receive antibiotics within 60 minutes of skin incision; (2) 8% of patients had inadequate postoperative dosing; and (3) 27% of eligible patients did not receive intraoperative redosing. As the duration of antibiotic prophylaxis was governed by the presence of chest tubes in the preintervention period, as expected, only 38% of subjects had antibiotics discontinued within 48 hours of surgery or within 24 hours of chest closure. During the postintervention period, compliance with the 4 process of care measures significantly improved.

Table 1. Protocol for Perioperative Antibiotic Prophylaxis for Neonatal Cardiac Surgery and Process of Care Measures

<table>
<thead>
<tr>
<th>Surgical Approach, Open or Closed Sternum</th>
<th>Pre and Intraoperative Antibiotic Prophylaxis</th>
<th>Postoperative Antibiotic Prophylaxis</th>
<th>Duration of Antibiotic Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac surgery through lateral thoracotomy or median sternotomy, closed sternum</td>
<td>Cefazolin: 30 mg/kg/dose Given in the OR within 60 minutes prior to skin incision. Repeat dose in 4 hours if surgical procedure exceeds 4 hours. Use vancomycin 15 mg/kg/dose (Administer up to 120 minutes prior to skin incision) if known colonization/infection with MRSA</td>
<td>Cefazolin: 30 mg/kg/dose ≤7 days old: q 12hours &gt;7 days old: q 8 hours</td>
<td>Discontinue antibiotics 48 hours after surgery end time.</td>
</tr>
<tr>
<td>Cardiac surgery, open sternum</td>
<td>Cefazolin 30 mg/kg/dose Given in the OR within 60 minutes prior to skin incision Repeat dose in 4 hours if surgical procedure exceeds 4 hours. Use vancomycin 15 mg/kg/dose (Administer up to 120 minutes prior to skin incision) if known colonization/infection with MRSA</td>
<td>Vancomycin: 15 mg/kg/dose ≤7 days old: q 12 hours &gt;7 days old: q 8 hours if known colonization/infection with MRSA.</td>
<td>Discontinue antibiotics 24 hours after sternal closure</td>
</tr>
</tbody>
</table>

MRSA = methicillin resistant Staphylococcus aureus; OR = operating room; q = every.
and generally exceeded 90% (Table 3). However, postoperative drug dosing remained suboptimal; only 65% of subjects received the recommended dose and underdosing of cefazolin was the most common deficiency (range, 5 to 26 mg/kg). Compliance with appropriate antibiotic prophylaxis was similar among subjects with and without SSIs (Table 4).

Comment
To our knowledge, this is the first study to investigate the impact of a standardized perioperative antibiotic prophylaxis protocol for neonatal cardiac surgery. We focused on neonates because they are at greater risk for SSIs than older children and adults [2, 4, 7]. Furthermore, no recommendations exist for perioperative antibiotic prophylaxis after neonatal cardiac surgery. The American Society of Health-System Pharmacists report offers recommendations for cardiac surgical antibiotic prophylaxis after neonatal cardiac surgery. The RACHS-1 = risk adjustment in congenital heart surgery.

We confirmed our hypothesis that adult guidelines were safe to use in neonates. Limiting the duration of perioperative antibiotic prophylaxis to 48 hours in neonates with a closed sternum did not increase SSI rates in our study. The 6% rate of SSI in our study population is within the range reported in other studies; however, those studies also included older children [2–7]. Our results are similar to studies of adult and pediatric cardiac surgical patients wherein no incremental benefit was noted for extending prophylaxis beyond 48 hours or until chest tubes or invasive catheters and vascular lines were removed [18, 25]. However, our findings differed from those reported by Maher and colleagues [20] wherein limiting prophylaxis to 48 hours increased the rate of SSI in pediatric cardiac surgical patients compared with when guided by the presence of thoracotomy tubes and vascular catheters.

Recommendations for perioperative prophylaxis have been proposed by several national organizations, including the Society of Thoracic Surgeons, and all discourage the extended use of antibiotic prophylaxis.
Prolonged antibiotic administration carries the hazard of promoting growth of resistant bacterial strains or yeast, or developing Clostridium difficile colitis or other toxicities without substantially decreasing infectious risk [11, 13, 18, 25]. However, surveys of practice have revealed that prolonged antibiotic prophylaxis is common practice in pediatric cardiac surgery; 40% of surgeons continued antibiotic prophylaxis beyond 24 to 48 hours after surgery and 30% of centers continued prophylaxis until chest tube removal [15–17]. We speculate several reasons why caregivers are reluctant to limit perioperative antibiotic prophylaxis duration. Most neonatal cardiac surgeries are performed on cardiopulmonary bypass, which has detrimental effects on cellular and humoral response [26]. Furthermore, the mortality rate is greatly increased in patients who develop organ space SSIs [27]. Invasive devices do increase the risk of health care associated infections but there is no evidence that perioperative prophylaxis reduces this risk.

No guidelines exist for antibiotic prophylaxis for patients who have an open sternum postoperatively. Hence, different antibiotic regimens are used and often for extended durations [15–20]. Our study did not find a difference in SSI rates in neonates in the preintervention and postintervention periods.

Table 3. Comparison of Perioperative Antibiotic Prophylaxis Compliance Process Measures in the Preintervention and Postintervention Periods

<table>
<thead>
<tr>
<th>Performance Measure</th>
<th>Preintervention Period</th>
<th>Postintervention Period</th>
<th>p Value</th>
<th>OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perioperative prophylaxis given</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>138 (95)</td>
<td>137 (99)</td>
<td>0.07</td>
<td>0.14</td>
</tr>
<tr>
<td>Intraoperative re-dosing, n = 131</td>
<td>44/60 (73)</td>
<td>70/71 (99)</td>
<td>&lt;0.01</td>
<td>0.04</td>
</tr>
<tr>
<td>Postoperative</td>
<td>141 (97)</td>
<td>136 (99)</td>
<td>0.68</td>
<td>0.52</td>
</tr>
<tr>
<td>Correct drug</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>132 (96)</td>
<td>134 (98)</td>
<td>0.50</td>
<td>0.49</td>
</tr>
<tr>
<td>Postoperative</td>
<td>124 (88)</td>
<td>133 (98)</td>
<td>&lt;0.01</td>
<td>0.16</td>
</tr>
<tr>
<td>Correct dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>115 (87)</td>
<td>124 (93)</td>
<td>0.14</td>
<td>0.55</td>
</tr>
<tr>
<td>Postoperative</td>
<td>20 (16)</td>
<td>86 (65)</td>
<td>&lt;0.01</td>
<td>0.11</td>
</tr>
<tr>
<td>Correct timing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>106 (80)</td>
<td>132 (99)</td>
<td>&lt;0.01</td>
<td>0.06</td>
</tr>
<tr>
<td>Postoperative</td>
<td>39 (89)</td>
<td>66 (94)</td>
<td>0.30</td>
<td>0.47</td>
</tr>
<tr>
<td>Correct discontinuation</td>
<td>47 (38)</td>
<td>126 (95)</td>
<td>&lt;0.01</td>
<td>0.03</td>
</tr>
</tbody>
</table>

CI = confidence interval; OR = odds ratio.

Table 4. Perioperative Antibiotic Prophylaxis Process Measures and SSI

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SSI n = 17 (%)</th>
<th>No SSI n = 266 (%)</th>
<th>p Value</th>
<th>OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics given</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>16 (94)</td>
<td>259 (97)</td>
<td>0.39</td>
<td>0.43</td>
</tr>
<tr>
<td>Intraoperative, n = 131</td>
<td>7/9 (78)</td>
<td>107/122 (88)</td>
<td>0.24</td>
<td>0.49</td>
</tr>
<tr>
<td>Postoperative</td>
<td>17 (100)</td>
<td>260 (98)</td>
<td>0.69</td>
<td>-</td>
</tr>
<tr>
<td>Correct drug</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>16 (100)</td>
<td>250 (97)</td>
<td>0.58</td>
<td>-</td>
</tr>
<tr>
<td>Postoperative</td>
<td>16 (94)</td>
<td>241 (93)</td>
<td>0.38</td>
<td>1.26</td>
</tr>
<tr>
<td>Correct dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>15 (94)</td>
<td>224 (90)</td>
<td>0.33</td>
<td>0.57</td>
</tr>
<tr>
<td>Postoperative</td>
<td>6 (38)</td>
<td>100 (41)</td>
<td>0.20</td>
<td>0.85</td>
</tr>
<tr>
<td>Correct timing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>13 (81)</td>
<td>225 (90)</td>
<td>0.23</td>
<td>2.08</td>
</tr>
<tr>
<td>Intraoperative</td>
<td>7 (100)</td>
<td>98 (92)</td>
<td>0.55</td>
<td>-</td>
</tr>
<tr>
<td>Correct discontinuation</td>
<td>12 (75)</td>
<td>161 (67)</td>
<td>0.18</td>
<td>1.49</td>
</tr>
</tbody>
</table>

CI = confidence interval; OR = odds ratio; SSI = surgical site infection.
SSIs in adult populations [28–30]. During the preintervention period only 80% of neonates who underwent surgery received antibiotic prophylaxis within 60 minutes of skin incision. Furthermore, about 25% of neonates who were candidates for re-dosing did not receive an additional dose of antibiotics in the operating room. We also found that despite quarterly audits and feedback to key stakeholders including the cardiothoracic surgical team, neonatal cardiac care team, and anesthesiologists, postoperative dosing of cefazolin remained suboptimal in the postintervention period, as infants were frequently underdosed. We speculate that a default dosing recommendation in our electronic medical record or the use of an incorrect weight for dose calculations by providers likely contributed to suboptimal dosing.

Several methods including hospital collaboratives, electronic medical records, and order sets have been employed to improve SIP performance measures in adult surgical patients [29, 30]. Our study confirms the importance of antibiotic stewardship programs and dedicated interdisciplinary task forces in improving adherence to these process measures. Periodic audits, feedback, and education to prescribers and key stakeholders significantly improved the selection, dosing and timing, and discontinuation of prophylactic antibiotics in our study.

Despite improved adherence to perioperative antibiotic prophylaxis measures in the postintervention period, a statistically significant decline in SSI rate was not noted in our study, although a higher proportion of complex cases were performed. Studies evaluating the effectiveness of SIP process measures on reducing SSI rates in adult surgical patients have generated conflicting results [30–32]. While some studies have shown a decline in SSI rates with improved adherence to process measures, others have not demonstrated a similar benefit [30–32]. Factors other than appropriate delivery of perioperative antibiotic prophylaxis may also influence SSI rates including hospital case volume, case-mix index, surgical skill, working environment, and overall quality of care [31, 32].

Our study did not find significant differences in rates of compliance with any of the 4 process measures between neonates who developed SSI and those who did not develop SSI. These results appear to contradict our earlier finding that incorrect timing of preoperative antibiotic prophylaxis was a risk factor for SSI after cardiac surgery [22]. We speculate that several differences in study design may account for these divergent findings. The previous study was conducted between January 2010 and December 2011, included all infants younger than 1 year of age, and analyzed outcomes after 552 procedures. Thus, the sample size of the current study may have been too small to detect an association between incorrect preoperative timing of prophylactic antibiotic and SSI. It is also possible that factors other than appropriate perioperative prophylaxis influence SSI rates in neonates.

There are several limitations to this study. This is a single-center study with a unique, cardiac NICU and thus the findings may not be generalizable to other pediatric cardiac ICUs in which care is offered to older children in the same unit. Although the proportion of patients who received appropriate perioperative antibiotic prophylaxis increased significantly during the postintervention period, the decline in the incidence of SSI during this period was not statistically significant. The sample size may be too small or the study period may be too short to see a statistically significant decrease in the rate of SSI. Furthermore, SSI may not have been reported if patients presented to other institutions.

In conclusion, this study demonstrates that limiting the duration of perioperative antibiotic prophylaxis for neonatal cardiac surgery to 48 hours if the sternum is closed or to 24 hours after sternal closure is safe as determined by SSI rates. Additional multicenter studies are needed to develop national guidelines for perioperative prophylaxis for this population. The implementation of the consensus protocol with feedback resulted in significant improvements in the delivery of perioperative antibiotic prophylaxis in 4 process measures including appropriate drug selection and dosing, timely administration, and discontinuation. However, deficiencies in postoperative dosing persisted in the postintervention period. Further research is needed to determine the association between each of the perioperative antibiotic prophylaxis process of care measures and the occurrence of SSI.

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References


